Remarks

Amendments

1. Please amend claim 40 as shown on the attached pages. Claim 40 has been amended to clarify the steps of the claimed method. New claim 51 has been added (supported for instance in [0010] and [0047] of US 2007/0298120). A typographical amendment has been effected in claim 46.

Claims Rejection – 35 USC § 112

2. Claims 40-50 were rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner contends that the phrase "optionally under photo-activation by UV radiation" (appearing in claim 40) renders the claims indefinite because it is unclear whether the photo-activation step is necessary for the AzRu to bind to calcium ion binding protein.

The Applicant respectfully draws the Examiner's attention to amended claim 40, which now recites as follows:

> 40. A method for inhibiting the calcium-binding activity of a Ca^{2+}-binding protein, comprising
>
> i) providing a photoreactive azido-ruthenium (AzRu) compound which contains in its molecule ruthenium, azido group, and chlorine in the molar ratio of 2:1:5;
>
> ii) contacting said Ca^{2+}-binding protein with said AzRu compound, in order to inhibit the calcium-binding activity of said Ca^{2+}-binding protein bind; **and optionally**
>
> iii) applying UV irradiation for covalently binding said AzRU compound to said Ca^{2+}-binding protein.

A person skilled in the art, reading the above claim, would easily understand that steps i) and ii) are required and sufficient to inhibit the calcium-binding activity of a Ca^{2+}-binding protein. However, step iii) may be used to covalently bind the AzRu compound to the target protein, thereby inhibiting the activity of said protein in an irreversible manner.

It is believed that the amendments effected in claim 40 render the Examiner's rejection moot, the same being applied to claims 41-50, which are all dependent from claim 40. Therefore, amended claims 40-50 now fully comply with the provisions of 35 USC § 112.

Claims Rejection – 35 USC § 103

3. Claims 40-46 have been rejected as being unpatentable over Ying et al. (Biochem. 30:4949-4952, 1991, hereafter "**Ying**") in view of Brown et al. (Inorganic Chemistry, 14(8):1915-1921, 1975, hereafter "**Brown**"). Claims 47-50 are further rejected as being unpatentable over Ying in view of Brown as applied to claim 40, and further in view of Harverstick et al (Cancer Research, 60:1002-1008, 2000, hereafter "**Harverstick**"). The Applicant respectfully traverses the Examiner's rejection for the following reasons.

With regard to claim 40, the Examiner notes that **Ying** teaches ruthenium red as being a well known and effective inhibitor of the mitochondrial calcium ion, but acknowledges that said publication does not teach a photoreactive azidoruthenium (page 4, paragraph 8 of the Office Action). Therefore, the Examiner adds **Brown** as a secondary reference, alleging that said publication teaches a mixture of $Ru(bipy)_2Cl_2$ suspended in water containing 46 mmol of sodium azide which would correspond to a photoreactive compound as recited in claim 40, namely a compound containing ruthenium, azido group and chlorine in a molar ratio of 2:1:5 (page 4, paragraph 9 of the Office Action). However, the Examiner admits that neither **Ying** nor **Brown** teaches inhibiting, treating, or mitigating a disorder associated with a defect in the function of a calcium ion binding protein (page 5, paragraph 14 of the Office Action). Therefore, the Examiner further cites **Harverstick**, noting that said publication relates to the inhibition of human prostate cancer proliferation by blocking the receptors for calcium ion (page 5, paragraph 15 of the Office Action).

In response to the above-specified objection, the Applicant respectfully submits the Examiner errs when contending that the compounds of **Brown** correspond to the one disclosed in instant claim 40. A careful reading shows that **Brown** indeed relates to **Azido(bis-2,2'bipyridine) complexes of Ruthenium** of general formula Ru(bipy)2(N3)2 and Ru(bipy)2(L)(N3)+, wherein "bipy" stands for 2,2'-bipyridine and "L" is either acetonitrile or pyridine (see abstract). An example of such a compound is disclosed for instance on page 1915, col.2, line 34, with the following formula: $RuC_{10}H_{18}N_{10}O$. A person skilled in chemistry understands that the compounds disclosed in **Brown** are radically different from those recited in instant claim 40, as they include **carbon atoms, one single ruthenium atom, and no chlorine atoms at all**. Therefore, the compounds of Brown do not satisfy the essential feature recited in claim 40, namely a molar ratio 2:1:5 between ruthenium, azido group, and chlorine.

Furthermore, it should be emphasized that not only **Brown** fails to teach the compound of claim 40, but a person skilled in the art, reading said publication, would not be motivated to produce such a compound. Should it have been the case, there is not even one single hint in **Brown** that would give a person skilled in the art reasonable expectations that such a compound would be successful in inhibiting the calcium-binding activity of Ca^{2+}-binding proteins.

As noted by the Examiner, **Harverstick** relates to the inhibition of human prostate cancer proliferation by blocking the receptors for calcium ion. Said publication does not relate to an azidoruthenium compound as disclosed in instant claim 40.

In view of the above, it is submitted that none of the above publications, taken alone or in combination, teaches or suggests the method recited in instant claim 40. It is well established that all words in a claim must be considered in judging the patentability of that claim against the prior art (In *re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970)). As no *prima facie* case of obviousness can be established against claim 40 based on the above cited prior art, it is the Applicant's belief that claim 40, as well as claims 41-50 which are all dependent therefrom, should be acknowledged as both novel and non-obvious.

4. Claims 40-46 have been further rejected as being unpatentable over Ying et al. (Biochem. 30:4949-4952, 1991, hereafter "**Ying**") in view of Douglas et al. (Journal of the American Society, 94(15):5254-5258, 1972, hereafter "**Douglas**"). Claims 47-50 are further rejected as being unpatentable over Ying et al. in view of Douglas et al.

as applied to claim 40, and further in view of Harverstick et al (Cancer Research, 60:1002-1008, 2000, hereafter "**Harverstick**"). The Applicant traverses the Examiner's rejection for the following reasons.

With regard to claim 40, the Examiner notes that **Ying** teaches ruthenium red as being a well known and effective inhibitor of the mitochondrial calcium ion, but acknowledges that said publication does not teach a photoreactive azidoruthenium (page 6, paragraph 18 of the Office Action). Therefore, the Examiner adds **Douglas** as a secondary reference, asserting that said publication teaches an azido-ruthenium compound which would correspond to a compound as recited in claim 40, namely a photoreactive compound which contains ruthenium, azido group and chlorine in a molar ratio of 2:1:5 (page 6, paragraph 19 of the Office Action). However, the Examiner admits that neither **Ying** nor **Douglas** teaches inhibiting, treating, or mitigating a disorder associated with a defect in the function of a calcium ion binding protein (page 7, paragraph 24 of the Office Action). Therefore, the Examiner further cites **Harverstick**, noting that said publication relates to the inhibition of human prostate cancer proliferation by blocking the receptors for calcium ion (page 7, paragraph 25 of the Office Action).

In response to the above-specified objection, the Applicant respectfully submits that the Examiner errs when contending that the compounds of **Douglas** correspond to those of the present invention. A careful reading shows that **Douglas**, among all the disclosed molecules, relates to a ***trans*-[$RuN_3Cl(das)_2$]** compound, wherein "das" stands for o-phenylenebis(dimethyl-arsine) (see page 5254, col.1, third paragraph), which comprises ruthenium, azido group, and chlorine. Similarly to the case of Brown et al. cited above (see point #3), a person skilled in the art of chemistry, easily understands that **Douglas** does not relate at all to the compound appearing in instant claim 40. The closest compound disclosed in **Douglas** is radically different from the one of claim 40 and includes **carbon atoms (from the "das" chemical group), one single ruthenium atom, and one chlorine atom**. Therefore it is clear that the compound of **Douglas** does not disclose a molar ratio 2:1:5 of Ru:Azido group:Chlorine, as recited in the method of instant claim 40.

It should also be highlighted that, beside **Douglas** failing to teach the compound used in the method of claim 40, a person skilled in the art, reading said publication, would not be motivated to produce such a compound. Should it have been the case, there is not one single hint in **Douglas** that would provide a person skilled in the art reasonable expectation that such a compound would be successful in inhibiting the calcium-binding activity of Ca^{2+}-binding proteins.

As noted by the Examiner, **Harverstick** relates to the inhibition of human prostate cancer proliferation by blocking the receptors for calcium ion. Said publication does not relate to an azidoruthenium compound as disclosed in instant claim 40.

In view of the above, it is submitted that none of the above publications, taken alone or in combination, teaches or suggests the method recited in instant claim 40. It is well established that all words in a claim must be considered in judging the patentability of that claim against the prior art (In *re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970)). As no *prima facie* case of obviousness can be established against claim 40 based on the above cited prior art, it is the Applicant's belief that claim 40, as well as claims 41-50 which are all dependent therefrom, should be acknowledged as both novel and non-obvious.

Conclusion

5. As it is believed that all the rejections set forth in the Office Action have been fully addressed by the amendments and the above explanations, favorable reconsideration and allowance of the claims are earnestly solicited.

Respectfully submitted

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